Journal of Current Hematology & Oncology Research

Case Report

DOI: 10.51271/JCHOR-0066

A rare case report: cytarabine-induced skin rash

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Cite this article: Gülsar Çaycı MG, Satılmış O, Demircioğlu S, Tekinalp A. A rare case report: cytarabine-induced skin rash. *J Curr Hematol Oncol Res.* 2025;3(3):74-76.

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Received: 12/03/2025 ◆ **Accepted**: 09/04/2025 ◆ **Published**: 08/08/2025

ABSTRACT

Cytarabine, a commonly used antimetabolite in hematologic malignancies, has various side effects, including dermatological toxicity. A 61-year-old male with relapsed diffuse large B-cell lymphoma (DLBCL) was started on the MATRIX regimen, including high-dose cytarabine. On the third day of treatment, he developed a palmar rash, which later progressed to petechiae and purpura on the trunk, back, and lower extremities. No systemic corticosteroid treatment was administered, and the rash gradually resolved by the 13th day. This case highlights a rare dermatological reaction to cytarabine. Although cutaneous toxicity of cytarabine is uncommon, clinicians should be aware of its potential manifestations and manage patients symptomatically to avoid unnecessary interventions while ensuring treatment continuation.

Keywords: Chemotherapy, cytarabine, palmar-plantar erythema, generalized exanthematous pustulosis

INTRODUCTION

Non-Hodgkin lymphoma (NHL) is the most common hematological malignancy, with B-cell lymphomas constituting the majority of cases. Diffuse large B-cell lymphoma (DLBCL) is the most frequently observed histological subtype, accounting for approximately 30% of newly diagnosed cases annually.[1] In Turkiye, based on 2014 data, the incidence of DLBCL is 6 per 100.000 people.[2] It is slightly more common in males than in females (male/female ratio=1.5).[3]

The first-line treatment for DLBCL patients is the CHOP protocol, which is combined with the Anti-CD20 monoclonal antibody rituximab and administered every 21 days as the standard regimen.

For relapsed or refractory DLBCL patients, autologous stem cell transplantation (ASCT) is the only option to achieve long-term remission. However, factors such as the patient's age, treatment-related morbidities, and low performance status may prevent the application of ASCT in all cases. For patients who do not respond to first-line treatment, salvage regimens such as R-ICE, R-DHAP, or MATRIX protocols may be used. Clinical studies have reported no significant difference in relapse rates among these regimens. Therefore, salvage therapy should be selected based on individual patient evaluations to determine the most appropriate protocol.

Cytarabine treatment can lead to cardiovascular, dermatological, gastrointestinal, hepatic, and immunological side effects. A review of the literature indicates that cytarabine can cause severe dermatological toxicity.[4,5] Dermatologic reactions include acute generalized exanthematous pustulosis, alopecia, dermal ulcers, efflorescence, pruritus, skin rashes and urticaria. However, rashes affecting the palmar surface due to cytarabine treatment are quite rare. This report presents a case of a patient who developed a drug eruption starting with a palmar rash following cytarabine treatment during the MATRIX regimen, administered after a CNS relapse in a patient previously treated with R-CHOP.[6]

CASE

A 61-year-old male patient presented with dyspeptic complaints and was diagnosed with DLBCL following a gastric biopsy. He underwent six cycles of the R-CHOP chemotherapy protocol. After treatment, he was considered to be in remission and placed under follow-up. Notably, the patient had developed erythema during the R-CHOP regimen, which resolved without sequelae.

During remission follow-up, the patient presented to the emergency department with altered consciousness, vision loss, and speech impairment. Imaging revealed a 22×20 mm mass measuring in the left temporal lobe. A total excision of the mass was performed by neurosurgery. Upon pathological examination revealing DLBCL infiltration of the mass, the patient was referred to us with a diagnosis of central nervous system (CNS) lymphoma relapse. The patient, who

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had previously received 6 cycles of R-CHOP chemotherapy, was subsequently initiated on the MATRIX chemotherapy regimen. This protocol included methotrexate 850 mg/day on the first day, followed by cytarabine 3400 mg twice daily on the second and third days.

On the third day of treatment, shortly after the completion of intravenous cytarabine infusion, the patient developed lesions on the palms and perioral area (**Figure 1**). At the same time, he experienced subfebrile fever. However, no symptoms suggestive of Cytarabine syndrome such as myalgia, bone pain, chest discomfort, conjunctival irritation, or severe fatigue were observed during the clinical course. On the 7th day of treatment, the lesions spread, becoming more prominent as petechiae and purpura, with greater intensity on the palms and less intensity on the trunk, back, and lower extremities. These lesions were non-pruritic and painless (**Figure 2, 3**).

Figure 1. Lesions that developed on the palms after the completion of the intravenous cytarabine dose on the 3rd day of treatment

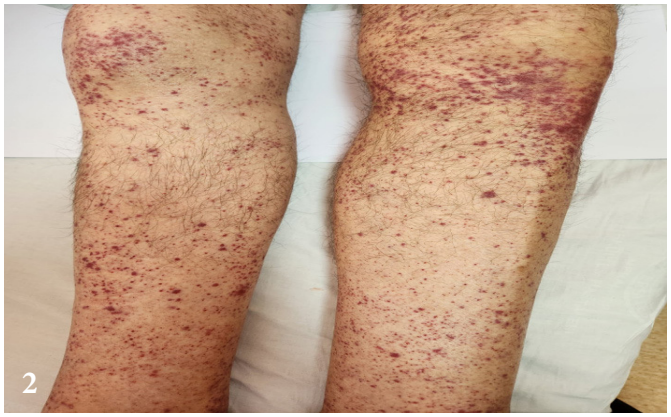

Figure 2 and 3. Non-pruritic and painless petechiae and purpura that developed on the trunk, back, and lower extremities on the 7th day of treatment

Upon the development of cutaneous lesions, a dermatology consultation was requested. Antinuclear antibody (ANA) and extractable nuclear antigen (ENA) antibody tests were performed to rule out leukocytoclastic vasculitis. As the test results were negative, a subsequent rheumatology consultation was obtained, and the preliminary diagnosis of vasculitis was excluded. Dermatology recommended topical treatment with a carbamide-containing emollient for hydration and a methylprednisolone aceponate-containing pomade for the affected areas. During this period, neither oral nor intravenous steroid treatment was administered. The lesions responded well for optimal clinical management to treatment, with the petechiae and purpura beginning to fade by the fourth day after onset (day 13 of treatment) (**Figure 4**).

Figure 4. Petechiae showing signs of fading on the 13th day of treatment

Resolution of the lesions following topical treatment and completion of the chemotherapy regimen supported the diagnosis of a drug-induced skin eruption.

The patient provided written informed consent for the publication of this case report and accompanying images.

DISCUSSION

DLBCL is one of the most common subtypes of hematologic malignancies and requires a multidisciplinary approach due to its aggressive course. In this case, we discuss the development of a cutaneous reaction following cytarabine-containing MATRIX chemotherapy in a patient presenting with CNS relapse of DLBCL.

Cytarabine is a widely used antimetabolite in the treatment of hematologic malignancies, acting by inhibiting DNA synthesis during the S phase of cell division. However, dermatologic side effects of this drug are rarely reported. In the literature, the most frequently reported dermatologic reactions associated with cytarabine include a broad spectrum of manifestations such as palmar-plantar erythrodysesthesia, morbilliform rashes, and acute generalized exanthematous pustulosis.[1,7] While skin rashes are common in cytarabine treatment, palmar erythema and similar skin eruptions are rare. A few cases in the literature have reported similar symptoms. Specifically, the development of palmar rashes or petechiae/purpura is rare but has been documented. In our case, the appearance of petechiae and purpura starting in the

palmar-plantar region and spreading to the trunk and lower extremities after intravenous cytarabine administration exemplifies the drug's toxic effects on the skin.

Cytarabine-induced cutaneous toxicities generally follow a benign course and tend to resolve spontaneously. Literature reports indicate that symptoms generally emerge within 2–8 days after treatment initiation and regress within 1–2 weeks.[1,7] Similarly, in our case, the rash began on the third day of treatment and showed signs of fading by the 13th day. The fact that the patient's symptoms improved with only topical treatment, without the need for systemic corticosteroid therapy, supports the notion that cytarabine-induced skin lesions are usually asymptomatic and benign.

Previous studies have identified a correlation between cytarabine dosage and dermatologic reactions. Particularly in patients receiving high-dose cytarabine, more severe skin toxicities have been reported; however, these findings have been observed to decrease with repeated doses.[7] Additionally, the causes of skin manifestations are multifactorial and may not be solely attributed to cytarabine, as other agents used in combination therapy can contribute to their occurrence. For example, a 2017 study by Karol et al.[8] reported that the combination of cytarabine and methotrexate could exacerbate skin reactions.

Vasculitis-like findings during cytarabine treatment are rare, and the exact pathogenesis of such reactions remains unclear.[1] In our case, vasculitis was considered a possible diagnosis following dermatology consultation. However, the absence of positive rheumatologic markers and other systemic symptoms suggested that the rash was specifically related to cytarabine.

CONCLUSION

As a result, although cutaneous reactions associated with cytarabine therapy generally follow a benign course, careful evaluation of such adverse effects is essential for optimal clinical management. Avoiding unnecessary tests and providing appropriate symptomatic treatment may allow continuation of therapy without negatively impacting the patient's prognosis.

This case underscores the importance of recognizing drug-induced cutaneous reactions that may develop during chemotherapy. Clinicians should be aware that drug-induced skin eruptions may occur during cytarabine-based chemotherapy and collaborate with dermatology specialists to ensure timely and appropriate management.

ETHICAL DECLARATIONS

Informed Consent
The patient signed and free and informed consent form.

Referee Evaluation Process
Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Financial Disclosure
The authors declared that this study has received no financial support.

Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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